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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,027	10/01/2004	Jean-Pierre Evenou	TX/4-32435A	4646

1095 7590 02/17/2006

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
BARKER, MICHAEL P	
ART UNIT	**PAPER NUMBER**
1626	

DATE MAILED: 02/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/510,027	EVENOU ET AL.	
	Examiner	Art Unit	
	Michael P. Barker	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-10* is/are rejected.

7)☒ Claim(s) *2,4,6 and 7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/1/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-10 are pending in this application.

Priority

This application, filed October 1, 2004, is a 371 of PCT/EP03/03470. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copies of UK Application No. 0207729.5, filed April 3, 2002 and UK Application No. 0303323.0, filed on February 13, 2003, have been filed.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on October 1, 2004 was correctly filed. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. Please refer to Applicant's copy submitted herewith.

Claim Rejections - Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and **3-10** ("instant claims") are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over **Claims 1-4** and **6-13** of U.S. Patent No. 6,645,970, issued November 11, 2003 ("conflicting claims"). Although the conflicting and instant claims are not identical, they are not patentably distinct from each other because the '970 patent claims compounds which are obvious variants of certain of the compounds in the instant claims. The obviousness-type double patenting rejection applies the same test as that of the 35 U.S.C. 103(a) rejection. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

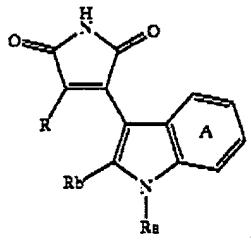
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

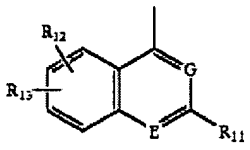
The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 and **3-10** rejected under Obviousness-type Double Patenting as being obvious over **Claims 1-4** and **6-13** of U.S. Patent No. 6,645,970, issued November 11, 2003.

1. Determining the scope and contents of the prior art

Conflicting **Claims 1-4** and **6-13** of U.S. Patent No. 6,645,970 disclose compounds of the general formula,  , wherein:

- **R** is 
- $\mathbf{R_a}$ is H or C_{1-4}alkyl;
- $\mathbf{R_b}$ is H or C_{1-4}alkyl
- $\mathbf{R_{11}}$ is a heterocyclic group; and
- $\mathbf{R_{12}}$ and $\mathbf{R_{13}}$ are independently H and C_{1-4}alkyl

or a salt thereof.

2. Ascertaining the differences between the prior art and the claims at issue

As interpreted through Examples 181, 182, 188, and 191 of the '970 patent, the compounds differ from those compounds of the instant claims by the substitution of a hydrogen for a methyl, or vice versa.

3. Resolving the level of ordinary skill in the pertinent art

It is well established that the substitution of methyl for hydrogen on a known compounds is not a patentable modification absent a showing of unexpected or unobvious results. In re Wood, 199 USPQ 137 (C.C.P.A. 1978). The motivation to make the claimed compounds derives

from the expectation of one skilled in the chemical art that structurally similar compounds would possess similar activity.

4. Considering objective evidence present indicating obviousness or nonobviousness

Evidence present in the '970 patent indicating obviousness can be found through the exemplification of species which vary from certain of the instantly claimed compounds by the substitution of a methyl for hydrogen, and vice versa. Namely, the overlapping examples are: Example 181, col. 29; Example 182, col. 30; Example 188, Table 7, col. 31; and Example 191, Table 7, col. 32.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 9 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for some disorders or diseases mediated by T lymphocytes and/or PKC or GSK-3β, these claims do not reasonably provide enablement for every disorder or disease mediated by T lymphocytes and/or PKC or GSK-3β. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

As stated in MPEP 2164.01(a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue."

In re Wands, set forth the following eight factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph:

1. The nature of the invention;
2. The state of the prior art;
3. The predictability or lack thereof in the art;
4. The amount of direction or guidance present;
5. The presence or absence of working examples;
6. The breadth of the claims;
7. The quantity of experimentation needed; and
8. The level of the skill in the art.

8 USPQ2d 1400 (1988).

The nature of the invention

The nature of the invention is a "method for preventing or treating disorders or diseases mediated by T lymphocytes and/or PKC or GSK-3β".

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art, pharmacology, involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. Because of the nature of unpredictability, it is highly unlikely that the contemporary knowledge in the art would allow one of ordinary skill in this art to accept the instantly claimed compounds or pharmaceutical compositions thereof as preventing or treating any disease or disorder mediated by T lymphocytes and/or PKC or GSK-3β.

The amount of direction or guidance present and presence or absence of working examples

There is no direction or guidance provided which supports Applicant's claimed method for the *preventing or treating* of *any* disease or disorder for which mediation of T lymphocytes and/or PKC or GSK-3β is/are indicated. The only direction or guidance present in Applicant's

Specification for a method for using compounds and compositions of Formula I to treat clinical conditions in which a β_2-adrenoreceptor agonist is indicated is found on pp. 15-23.

Pages 20 and 22 of Applicant's Specification reference specific diseases which are mediated by T lymphocytes and/or PKC or GSK-3β. However, Applicant's Specification does not provide support for the use of indolylmaleimide deriviatives in treating *any* clinical condition in a mammal for which mediation of T lymphocytes and/or PKC or GSK-3β is indicated, nor does Applicant's Specification provide guidance or direction of the use of Applicant's claimed compounds in the *preventing* of diseases in which mediation of T lymphocytes and/or PKC or GSK-3β is indicated.

The breadth of the claims, quantity of experimentation, and level of skill in the art

Claim 9 is drawn (in part) to "A method for preventing or treating disorders or diseases mediated by T lymphocytes and/or PKC or GSK-3β. . ." In order to *prevent* a disease in which mediation of T lymphocytes and/or PKC or GSK-3β is indicated, one would need to precisely identify those subjects likely to acquire such a disease, administer Applicant's claimed invention, and then demonstrate that if the identified subject did not develop the disease, such an effect was the direct result of administration of the claimed invention.

While the level of the skill in the pharmaceutical art is high, the quantity of experimentation needed to enable one skilled in the art to use Applicant's claimed compounds in treating *any* disease in which mediation of T lymphocytes and/or PKC or GSK-3β is indicated is undue. With no direction or guidance from Applicant's Specification, one of skill in the art would need to determine every disease associated with T lymphocytes and/or PKC or GSK-3β, identify subjects with such diseases, administer Applicant's claimed invention, and then

demonstrate that if the identified subject showed signs of overcoming such a disease, such an effect was the direct result of administration of Applicant's claimed invention.

Because of the aforementioned reasons, a person of skill in the art could not practice the claimed invention herein, or a person of skill in the art could practice the claimed invention herein only with undue experimentation and with no assurance of success.

This rejection can be overcome by deleting the word "preventing" and incorporating into **Claim 9** specific diseases associated with reversible airways obstruction found throughout the Specification.

Claim Objections

Claims 4 and **6-7** are objected to under 37 CFR 1.75 as being a substantial duplicate of **Claim 1**. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Specifically, the language used in **Claims 4** and **6-7**, "for use. . ." does not add to or limit Claim 1 but is viewed merely as intended use.

Claim 2 is objected to for being dependent on a rejected base claim but is otherwise allowable.

References Cited

If a copy of a provisional application listed on the bottom portion of the accompanying Notice of References Cited (PTO-892) form is not included with this Office action and the PTO-892 has been annotated to indicated the copy was not readily available, the copy could not be readily obtained when the Office action was mailed. Should Applicant desire a copy of such a

provisional application, Applicant should promptly request the copy from the Office of Public Records (OPR) in accordance with 37 CFR 1.14(a)(1)(iv), paying the required fee under 37 CFR 1.19(b)(1). If a copy is ordered from OPR, the shortened statutory period for reply to this Office action will not be reset under MPEP § 710.06 unless Applicant can demonstrate a substantial delay by the Office in fulfilling the order for the copy of the provisional application. Where the applicant has been notified on the PTO-892 that a copy of the provisional application is not readily available, the provision of MPEP § 707.05(a) that a copy of the cited reference will be automatically furnished without charge does not apply.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael P. Barker whose telephone number is (571) 272-4341. The examiner can normally be reached on Monday-Friday 8:00 AM- 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699. The unofficial fax phone for this group are (571) 273-8300.

When filing a FAX in Technology Center 1600, please indicate the Header (upper right) "Official" for papers that are to be entered into the file, and " Unofficial" for draft documents and other communications with the PTO that are not for entry into the file of the application. This will expedite processing of your papers.

Communication via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by applicant and should be addressed to [joseph.mckane@uspto.gov]. All Internet e-mail communications will be made of

record in the application file. PTO employees will not communicate with applicant via Internet e-mail where sensitive data will be exchanged or where there exists a possibility that sensitive data could be identified unless there is of record an express waiver of the confidentiality requirements under 35 U.S.C. 122 by the applicant. See the Interim Internet Usage Policy published by the Patent and Trademark Office Official Gazette on February 25, 1997 at 1195 OG 89.

KAMAL A. SAEED, PH.D.
PRIMARY EXAMINER

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